UNFRIENDLY FUMES

In the early days of cigarette smoke awareness, scientists, politicians, and the American public focused on the health effects of smoking on the smoker. The general conclusion since then has been that smoking cigarettes, cigars, and pipes can cause a wide range of illnesses from lung cancer to heart disease. In response, cigarette packs now carry warnings from the Surgeon General, tobacco companies are no longer allowed to advertise on television or specifically to children, and more than two million Americans quit smoking every year.

Today, at least some of the focus has shifted to how the active smoker's fumes affect the nonsmoker's health. Environmental tobacco smoke, or ETS, is a mixture of smoke from two sources: mainstream, which the smoker exhales, and sidestream, which curls up from the ends of a burning cigarette, cigar, or pipe between puffs. Although it is made up of the same toxic constituents as mainstream smoke, sidestream smoke contains more unburned hydrocarbons and is a more potent mutagen on a weight basis. About 50 million adult Americans now smoke and their spouses, children, and coworkers are the most likely to be exposed to ETS.

For years, antismokers called cigarette smoke a nuisance, especially in public places, but now a growing number of studies say secondhand smoke also kills. One of the most controversial and comprehensive studies, a 1993 report by the EPA, claims that ETS is responsible for at least 3,000 lung cancer deaths in America each year. The EPA also estimates that 150,000–300,000 children under 18 months of age develop pneumonia or bronchitis from breathing secondhand smoke, mostly at home. Numerous new studies have also linked ETS to heart disease and other cancers.

"As a social issue based on science, it is gaining momentum," says Tom Houston, tobacco control coordinator in the science division of the American Medical Association. "It's no longer just an annoyance. Secondhand smoke exposes us to known carcinogens."

According to the EPA report, ETS is made up of more than 4,000 compounds, including many known or suspected human carcinogens and toxic agents such as tar, nicotine, carbon monoxide, ammonia, arsenic, acetone, benzo[*a*]pyrene, formaldehyde, carbon monoxide, benzene, toluene, and *N*-nitrosodimethylamine. As a result, the EPA report classified ETS as a Group A carcinogen, meaning there is sufficient evidence to show that it causes cancer in humans. Only 15 other pollutants carry this most hazardous label, including asbestos, radon, and benzene.

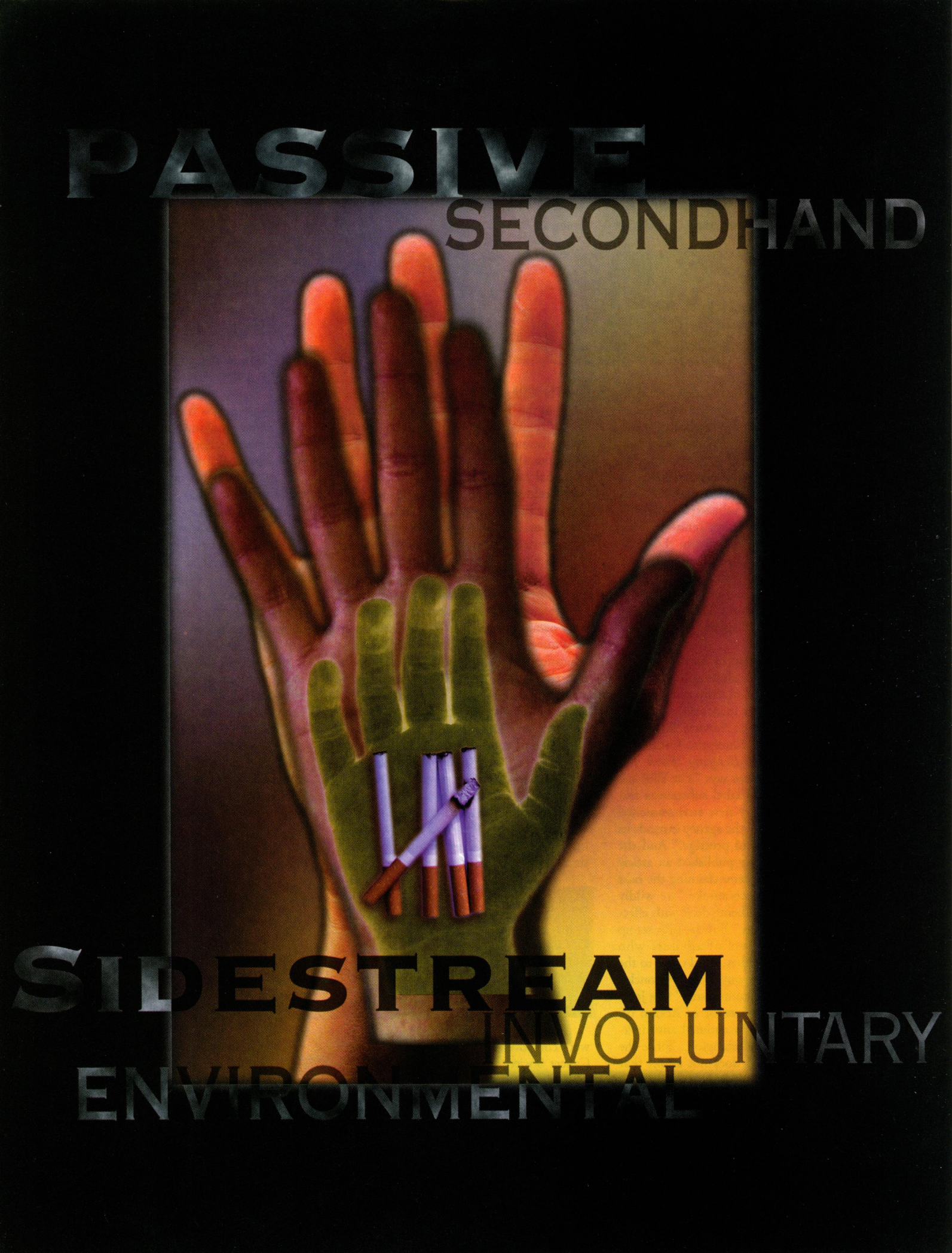
But not everyone agrees with the EPA's findings. As it has with other studies on the dangers of smoking, the tobacco industry responded by condemning the report and suing the agency. Among other criticisms, cigarette makers claim the EPA and the medical research community are biased in reporting on the health effects of secondhand smoke (this exposure is also called passive or involuntary smoking). They also accuse the agency of using only those reports that justify an antismoking position and of ignoring studies that might negate their arguments.

"It's getting to be a very emotive issue," says Chris Coggins, principal scientist and toxicologist in the research and development department at R.J. Reynolds Tobacco Company. "We contend that a number of the studies, largely epidemiological, that claim to show a tiny increase of risk in the nonsmoking wives of smokers, are flawed. There are many other confounders that could contribute to this risk. I look at the science involved and it's very weak. Just because you're married to a smoker doesn't mean you've breathed any of the smoke."

Disputed Evidence

The 1993 EPA report is the most frequently cited of all studies on the question of secondhand smoke. Estimating that most people spend 90% of their time indoors, and that U.S. smokers burn more than 400,000 tons of tobacco indoors each year, the EPA concluded that ETS "presents a serious and substantial public health risk." The report is based on the 30 then-available epidemiological studies comparing lung cancer rates in nonsmoking women whose husbands smoked with those in women whose husbands did not. Based on a total weight-of-evidence, rather than on any one study, the agency determined that the women married to smokers were at greater risk of developing lung cancer than those whose husbands did not smoke.

"The epidemiology data do not indicate a significant elevation in risk as a result of being married to a smoker or being exposed to ETS at work," writes Coggins in the R. J. Reynolds Tobacco Company's *Scientific Assessment of the EPA Report.* "ETS is hundreds to thousands (in some cases, millions) of times more diluted than is either mainstream or sidestream smoke. Eighty percent of the [report's] studies showed no statistically significant effect. It is therefore incon-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ceivable that public policy, calling for virtual bans on smoking, would be necessary to reduce exposure to such a negligible risk."

The EPA report builds on two earlier assessments of secondhand smoke by the National Research Council and the U.S. Surgeon General. In 1986, the NRC and the Surgeon General separately concluded that ETS can cause lung cancer in adult nonsmokers, that children of smokers are more likely to suffer from respiratory symptoms and lower respiratory tract infections, and that ETS is the leading source of indoor respirable suspended particulate matter.

It's no longer just an annoyance. Secondhand smoke exposes us to known carcinogens.

TOM HOUSTON, THE AMERICAN MEDICAL ASSOCIATION

"It isn't too astonishing that ETS can cause cancer because tobacco smoke is so clearly carcinogenic," says Jennifer Jinot, environmental health scientist in the EPA's Office of Research and Development. "What was surprising was that you could actually detect increased cancer risk in the epidemiological studies. The evidence of increasing risk with increasing exposure was especially compelling."

Although often cited by major American health and medical organizations, the EPA report has also been sharply criticized by conservative research institutions and the Congressional Research Service. For example, the Competitive Enterprise Institute in its *Environmental Briefing Book For Congressional Candidates* says "The EPA has a strong incentive to label substances carcinogenic. With every new environmental problem it 'discovers,' the agency expands its budget, influence, and prestige." And the Cato Institute recently published an article in its *Regulation Magazine* claiming the risks of secondhand tobacco smoke "are wildly exaggerated" and are "being dealt with effectively by private action." But the EPA set up an independent panel of advisers who reviewed the same evidence and came to the same judgment. "The only contrary conclusion is from the tobacco industry," says John Banzhaf, executive director of Action on Smoking and Health, a national antismoking group based in Washington. "Since the tobacco industry still does not admit that active smoking causes lung cancer, they obviously can't admit secondhand smoke causes cancer in the nonsmoker."

"We didn't discount any studies," says Jinot, who worked on the EPA report. "For people who are exposed at both home and work, home is generally the greatest single exposure. We didn't include the workplace data because there are problems in assessing exposure at the workplace over time because people change jobs and coworkers. And we looked at a lot of scientific data, not just the 30 epidemiological studies on ETS and lung cancer."

The EPA is not the only federal agency to point the finger at ETS as a health hazard. The Occupational Safety and Health Administration (OSHA) has classified ETS as a potential occupational carcinogen. The National Institute for Occupational Safety and Health has also recommended that ETS exposure in the workplace be reduced to the lowest possible levels.

The debate over secondhand smoke was slow to take hold, and began long after the controversy over active smoking. For years, most antismoking groups focused their efforts on convincing smokers to quit for their own health, and ETS was viewed more as a nuisance than a threat. Research and education efforts by prominent health organizations such as the American Lung Association (ALA), American Heart Association (AHA), and American Medical Association (AMA) were also focused on active smoking, in part because early evidence on ETS was "sparse and conflicting," according to *Consumer Reports*. In the early 1980s, two secondhand smoke studies conducted overseas showed that nonsmoking wives of heavy smokers had a higher risk of lung cancer than those whose husbands smoked less or not at all. But the findings were controversial, and even the American Cancer Society (ACS) did not accept them at the time, says Banzhaf.

"One of the most significant early studies was done in Japan," Banzhaf says. "There they compared two matched groups of housewives. This was significant because such a study is complicated in the United States, since so many women work outside of the home. In Japan, they tend to stay home much more, so any exposure would have to come from their husbands. The study showed that the [nonsmoking wives of smoking husbands] had a significant rate of lung cancer."

"We've looked more closely at the issue in recent years," says Clark Heath, vice president for epidemiology at the ACS. "Some of the earlier lack of excitement over ETS was because there was no clear risk to be seen from the available studies. Only in the last several years has there been enough follow-up."

"The major health organizations, including the AMA, were busy looking at other issues, like direct smoking, and passive smoking was less high on the priority list than active smoking," says Houston. "And the science was not yet as robust, not as easy to pin down. But the tobacco industry saw it coming. Passive smoking has emerged as one of the issues that has frightened the tobacco industry because they see nonsmokers saying they don't want to be exposed to thousands of chemicals. One internal tobacco industry document was called 'Here's a Cloud on the Horizon,' and recommended they do research that debunks the antismoking reports. But the number of studies has gained a lot of speed in the last few years."

In January 1991, the AHA reported that secondhand smoke kills 53,000 nonsmokers in the United States each year. In August 1994, the ALA reported that ETS led to about 47,000 heart disease deaths per year and 150,000 nonfatal heart attacks. In April 1995, a report in the *Journal of the American Medical Association* claimed that passive smoking appears to adversely affect the cardiovascular system and increase the risk of heart disease. The study said that ETS impedes the blood's oxygen-carrying capacity and interferes with the heart's ability to effectively use oxygen.

Children are especially vulnerable . . . A 40-pound child breathes more in a minute than a 160-pound man.

DAVID MANNINO, CENTERS FOR DISEASE CONTROL

"There seems to be a new study every week," says Coggins. "As a scientist, I step back and take an unbiased view. I look at the data, and they do not converge into a common point of view. The epidemiological studies are all over the place. There are probably about 40 to 45 now in the world, but most don't show anything at all. We consid-

er epidemiology as a blunt tool, not a fine analytical instrument. So using toxicological—rather than epidemiological—methods, we have done a number of studies on rats. And after controlling for variables and exposing them to very substantial levels of smoke, we saw no effects."

In March 1996, George Howard, biostatistician at the Bowman Gray School of Medicine in Winston-Salem, North Carolina, reported that the carotid arteries of passive smokers thicken at a faster rate than those of people not exposed to smoke. Howard's study, presented at an American Heart Association meeting, is considered the largest and possibly the first to show a direct link between secondhand smoke and the progression of atherosclerosis, a major cause of stroke. Researchers used ultrasound imaging to measure the progression of thickness, and reported an average 10% increase in the rate between five different groups, ranging from current smokers to nonsmokers.

"The thickness of the carotid artery is a fairly common indicator for atherosclerosis, or hardening of arteries," says Howard. "The walls get harder and thicker, which is linked to future heart disease. We found that the artery walls thickened by 20 micrometers between the nonsmokers and current smokers, a wonderfully straight dose–response. As a risk factor, the number of people exposed is large, and probably the most dosed group is the nonsmoking wife of a smoking husband."

In April, a Centers for Disease Control and Prevention (CDC) study reported that nearly 9 out of 10 nonsmokers had detectable amounts of cotinine, a metabolic residue from inhaled nicotine, in their blood. The results were based on samples from more than 10,000 Americans, ages 4 and older. Inhaled tobacco smoke is believed to be the only source of cotinine. This meant that the vast majority of nonsmokers had been exposed to tobacco smoke in the several days prior to testing. The CDC also reported that 43% of children and 37% of adult nonsmokers were exposed to ETS at home or work with an average exposure of four hours, per day based on a questionnaire sampling of nearly 17,000 Americans.

A July 1995 article in the *Journal of the American Medical Association* discusses the contradiction between what two major tobacco companies have publicly claimed about the apparent link between ETS and cancer and what their own internal reports conclude. While Brown & Williamson and the British American Tobacco Company (BAT) have denied that secondhand smoke causes cancer in nonsmokers, confidential company documents show that BAT researchers had discovered toxic agents in cigarette smoke years before the EPA report.

In refuting claims of harmful effects, tobacco companies often compare "cigarette equivalents," a method the EPA says has no scientific support. For example, in a full-page magazine advertisement, R. J. Reynolds Tobacco Company claimed that "a nonsmoker living with a smoker would, on average, be exposed to secondhand smoke equivalent to smoking approximately 1 1/2 cigarettes." In the fine print, however, the tobacco company acknowledges that the calculations are based on nicotine levels, which diminish rapidly in secondhand smoke, and that the measurement of "other compounds may give different results." The ad also acknowledges that using equivalent methods "are not necessarily relevant to an assessment of the potential risk from secondhand smoke."

A Decade of Detection

An early study of housewives in Japan shows that nonsmoking women whose husbands smoke have a significant rate of lung cancer.

In 1986, the National Research Council and the U.S. Surgeon General separately conclude that environmental tobacco smoke (ETS) can cause lung cancer in adult nonsmokers, that children of smokers are more likely to suffer from respiratory symptoms, and that ETS is the leading source of indoor respirable suspended particulate matter.

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In 1995, several studies estimate that maternal smoking accounts for 1,900 cases of Sudden Infant Death Syndrome a year.

An April 1995 report in *JAMA* claims that passive smoking appears to adversely affect the cardiovascular system and increase the risk of heart disease.

A July 1995 article in *JAMA* reports that two major tobacco companies deny that ETS can cause cancer in nonsmokers, although their own internal research supports the findings.

In December 1995, the U.S. Labor Department orders the Veterans Administration to pay workers' compensation benefits to the widower of a nurse who died of lung cancer after 18 years of treating patients at a VA hospital in Illinois.

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An April 1996 study by the University of Louisville reports that pregnant wives of smokers may pass traces of toxic tobacco chemicals and known carcinogens to thier unborn babies.

The American Academy of Otalaryngology-Head and Neck Surgery now tells its patients that exposure to ETS increases the number of ear infections and how long each one will last in children.

Children and ETS

Since the early 1970s, researchers have warned that children and infants are most at

risk from exposure to ETS, especially at home. They have higher rates of respiratory symptoms and respiratory tract infections, according to the NCI. More than 100 studies have linked secondhand smoke to pneumonia, bronchitis, coughs, middle ear infections, sore throats and colds, asthma, and sudden infant death syndrome [SIDS]. In 1995, several studies estimated that maternal smoking accounts for 1,900 SIDS cases a year, that smoking during pregnancy triples the risk of SIDS, and that infants are twice as likely to die of SIDS if exposed to secondhand smoke.

Just because you're married to a smoker doesn't mean you've breathed any of the smoke.

CHRIS COGGINS, RJ REYNOLDS TOBACCO COMPANY

"The linkage [of SIDS] with maternal smoking is well established," says a statement issued by the NCI. "Current evidence strongly suggests that infants whose mothers smoke are at an increased risk of dying of SIDS." The NCI recommends that smoking be eliminated from the environment of small children.

"A big chunk of illness in children is likely attributable to secondhand smoke," says David Mannino of the CDC. "Children are especially vulnerable for a number of reasons. For their body weight, they breathe more than adults, and have a higher minute ventilation for their size. For example, a 40-pound child breathes more in a minute than a 160-pound man. Children also can't move out of areas as easily as adults, they don't have the freedom. And since smoke irritates the inside of the lungs, a little bit of irritation goes a lot further in a child than in an adult."

The American Academy of Otolaryngology–Head and Neck Surgery tells its patients that approximately 26% of adults in the United States currently smoke cigarettes and that 50–67% of children under five live in homes with at least one adult smoker. The academy also says that exposure to ETS increases the number of ear infections and how long they last. Inhaled smoke irritates the Eustachian tube, which connects the back of the nose with the middle ear, causing swelling and obstruction that leads to pain, fluid, infection, and possible hearing loss, according to the academy.

"In the middle ear, the mechanisms for infection are not clear," says Houston. "However, the middle ear contains cilia like the lung, which can swell and close up when exposed to smoke. Because their tissues are in the early stages of development and rapid growth, they are more susceptible to all manner of toxins. So even though most people are well-meaning, it's not good enough for parents to confine their smoking to a bedroom or kitchen."

"The analogy I use is that it's like trying to chlorinate half of a pool," adds Mannino. "Smoke moves through the whole house, and houses are much tighter these days. Just sending the child to another room is not enough."

In April 1996, Steven R. Myers, a researcher at the University of Louisville reported that pregnant wives of smokers may pass traces of toxic tobacco chemicals and known carcinogens to their unborn babies, denying the long-held belief that the placenta blocks toxins from reaching the fetus. Researchers found traces of benzo[*a*]pyrene, 4-aminobiphenyl, linked to bladder cancer and now banned in industrial dyes, as well as acrylonitrile, which causes liver cancer, in the blood of newborns. Substance levels also rise dramatically when the mother is also a smoker. Myers presented his study at a meeting of the American Association for Cancer Research.

"A few years ago I worked in a hospital emergency room," says Mannino, a practicing pulmonary physician. "And I would see kids reeking with smoke having an asthma attack and their parents would be there smoking. Today, 55% of the adult patients in my practice have tobacco-related illnesses."

As a risk factor, . . . probably the most dosed group is the nonsmoking wife of a smoking husband.

GEORGE HOWARD, BOWMAN GRAY SCHOOL OF MEDICINE

In an April *USA Today* article, R. J. Reynolds Tobacco Company chairman Charles Harper was quoted as telling the company's shareholders, "If children don't like to be in a smoky room, they'll leave." When asked about infants, who can't leave a smoky room, Harper answered, "At some point, they begin to crawl." Harper later said he "meant that parents should be responsible for moving infants from smoky areas."

At Work, In Public Places, and Overseas

The battle over secondhand smoke is also being fought in communities and the courtroom. In December 1995, the United States Labor Department ordered the Department of Veterans Affairs to pay workers' compensation benefits to the widower of a nurse who died of lung cancer after 18 years of treating patients at a VA hospital in Illinois. Patients at the hospital were allowed to smoke freely and their rooms were often full of a "blue haze," according to an article in the *Detroit News*. Neither husband nor wife had smoked. It was the first workers' compensation award in the nation linking secondhand smoke to a cancer death.

Federal, state, and local legislatures continue to pass and strengthen bans on smoking in public places, including office buildings, restaurants, and parks. Nearly every state has enacted laws to protect nonsmokers, including some that require private employers to do the same. In addition, OSHA has proposed a government ban on smoking in most public businesses, including restaurants and casinos. Among other industry lobby groups, the National Restaurant Association and the Nevada Resort Association oppose the OSHA proposal.

Hundreds of towns and counties also restrict smoking, and most ordinances are more restrictive than those enacted by the states. Many municipal parks and recreations are now off-limits for smokers. In Davis and Palo Alto, California, smoking is banned within 20 feet of the entrance to a public building, making it virtually impossible for anyone to pause for a smoke in downtown areas; however, they may smoke if they keep walking. In New York City, smoking is no longer allowed in sports stadiums or park amphitheaters. In Fort Pierce, Florida, new tenants in public housing areas must sign an affidavit with their lease pledging not to smoke in their apartments.

As a result, smoke exposure has decreased dramatically in the past few decades. Says Mannino, "It's dropped from 70 percent in the 1970s to 37 percent now. And there is a huge difference between

[groups of different] socioeconomic status. The exposure rate is two times higher in lower socioeconomic groups, based on education and income."

In response to diminishing markets in the United States, tobacco companies have intensified their marketing efforts overseas. But though western Europe is generally considered a decade behind the United States in imposing smoking restrictions, it seems to be catching up. For example, France, England, Belgium, Denmark, Sweden, and Finland have banned smoking in some public places, including the Paris Métro and London Underground, and require no-smoking sections in restaurants. Such moves "imitate some of the excessive measures in the United States," Philip Morris spokesman Sean Murray said in a June article by the Associated Press.

Using the EPA's estimate that 3,000 people die each year from passive smoking, European Union health officials have recently intensified their criticism of the tobacco industry. In response, tobacco giant Philip Morris began a nine-country advertising campaign throughout western Europe that claims breathing secondhand smoke is less harmful than drinking whole milk.

Comparing medical research by different groups, the Philip Morris ads argue that passive smoke is less likely to cause lung cancer than drinking 1–2 glasses of whole milk each day, and that eating one cookie a day is more likely to cause heart disease than passive smoke is likely to cause lung cancer. But the British charity Cancer Research Campaign, which has reported that 4,000 people die each year in Europe because of passive smoke, calls the ads "an insult to our intelligence."

In May, *New Scientist* reported that a panel of European scientists denies passive smoking is a "primary lung carcinogen," contradicting the 1993 EPA report. Funded by the tobacco industry, the six-member panel insists its findings were not influenced by its sponsors. The panel claims the studies reviewed by the EPA were flawed because they were not controlled or randomized.

Elsewhere in the world, smoking regulations and bans have been gaining momentum. For example, São Paulo, Brazil, generally forbids smoking in restaurants, schools, buses, hospitals, and stores, except in special smoking sections. Smoking still meets few restrictions in Mexico and Asia, but many Canadian communities have imposed strict limitations on lighting up in public. In July, the City of Toronto voted to ban smoking in all public eating establishments as of January 1997, unless a bar or restaurant's owner can provide a separately ventilated and enclosed area for smokers. In making their decision, city council members determined that open nonsmoking areas provide little or no protection from exposure to secondhand smoke. At the same time, the Council declared its intent to make all public places in Toronto smoke-free by the year 2000.

The debate over secondhand smoke affects every aspect of American life, from the basic right to breathe clean air to the legal right to smoke. As researchers publish reports adding to the evidence on the multitude of health problems caused by secondhand smoke, legislatures pass ordinances protecting nonsmokers from exposure to ETS. As courts award compensation to victims, private businesses are ordering their smoking employees not to light up inside. And at the same time, the tobacco companies continue to try to convince the American public that the risk is negligible by attempting to refute data that show negative health effects.

"To have the evidence in hand that passive smoking harms health provides a powerful social tool to curtail smoking," says Heath. "And by discouraging passive smoking, this discourages active smoking. It's a very real-life maneuver to discourage active smoking."

"The bottom line for the AMA is that we're not just one organization with an axe to grind," says Houston. "Every health and science group has come to the same conclusion, and the weight of evidence is overwhelming. Clean air is as essential as clean water."

Rebecca Clay

Cancer Investigators Locate Smoking Gun

A study that purports to show the first evidence linking cigarette smoke to lung cancer at the molecular level may be the last bit of evidence needed by anti-tobacco groups to convince judges and juries that smoking kills. Cigarette manufacturers, however, deny that the findings are significant.

In the 18 October 1996 issue of *Science*, researchers at the M.D. Anderson Cancer Center in Houston reported that the tobacco carcinogen benzo(a)pyrene diol epoxide (BPDE) influences three molecular sites on the human *p53* gene, a gene that is critical in the development of cancer. "In essence, our study provides a direct link between a defined cigarette-smoke carcinogen and human cancer mutations," Moonshon Tang, a scientist at M.D. Anderson and lead author of the study said in a statement to the Associated Press. The study's other authors were Annie Pao, also of M. D. Anderson, and Mikhail F. Denissenko and Gerd P. Pfeifer of the Bechman Research Institute of the City of Hope in Durante, California.

BPDE is a chemical derived in the lungs from benzo(*a*)pyrene, a component of cigarette smoke that has been associated with lung cancer. Until now, however, the specific molecular reactions connecting BPDE to the formation of cancerous cells were unknown. Tang and his team attempted to rectify this situation by exposing human cells to BPDE and then mapping the specific sites where the chemical caused damage to the genetic material. The authors reported that the sites on the *p53* gene that were damaged by BPDE are exactly the same sites on that gene that are known to be mutated in lung cancer cells.

The *p53* gene, identified in 1990 as a key guardian against cancer, is responsible for ensuring that DNA is copied accurately during cell division. When the gene detects abnormal DNA, it halts the duplication or kills the cell. Damage to *p53*, such as that caused by BPDE, can inactivate this gene, thus allowing a cell with abnormal DNA to divide without restraint—a process that can lead to cancer.

According to John Banzhaf, director of an anti-tobacco group called Action on Smoking and Health, the study "helps to close a loophole" often used by lawyers claiming that tobacco manufacturers could not be held responsible for cancer in smokers because science had not proven that a precise biological process exists by which cigarette smoking causes lung cancer. However, cautions George Lucier, director of the NIEHS' environmental toxicology program, there are nearly 100 suspected carcinogens in cigarette smoke and the contribution of BPDE-induced *p53* mutations to smoking-mediated lung cancers is unknown and could be quite small.

The Brown & Williamson Tobacco Company issued a statement soon after the study was announced denying that the results necessarily indicate smoking as a particular cancer culprit. "Benzo(*a*)pyrene is everywhere," the statement said. "It is in the air, soil, and produced by the combustion of any kind of organic matter."